

Table S1. Plasma leucine, glucose, and insulin concentrations, and plasma α -ketoisocaproate (KIC), plasma leucine, muscle-free leucine, and muscle leucine tracer-to-tracee ratios (TTR) during the stable isotope infusion in the basal (postabsorptive) conditions, and during mixed meal feeding before and after 6-months of diet-induced weight loss plus different types of exercise interventions in obese older adults. See also Figure 2.

Control (N = 12)

Time (min)	Concentration								Enrichment (TTR)					
	Leucine (μ M)		Glucose (mg/dL)		Insulin (μ M/mL)		Plasma α -KIC		Plasma Leucine		Muscle-Free Leucine		Muscle Leucine	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Basal state														
0	123 ± 6	119 ± 9	116 ± 6	117 ± 6	17 ± 4	20 ± 5	-	-	-	-	-	-	-	-
30	-	-	-	-	-	-	0.0800 ± 0.0008	0.0839 ± 0.0015	0.0901 ± 0.0012	0.0893 ± 0.0014	-	-	-	-
40	-	-	-	-	-	-	0.0806 ± 0.0011	0.0804 ± 0.0013	0.0912 ± 0.0067	0.0910 ± 0.0014	-	-	-	-
50	-	-	-	-	-	-	0.0800 ± 0.0012	0.0809 ± 0.0011	0.0902 ± 0.0061	0.0921 ± 0.0017	-	-	-	-
60	128 ± 7	116 ± 8	122 ± 6	112 ± 7	20 ± 5	20 ± 5	0.0800 ± 0.0014	0.0804 ± 0.0011	0.0897 ± 0.0068	0.0928 ± 0.0017	0.0302 ± 0.0011	0.0329 ± 0.0021	0.001501 ± 0.000007	0.001550 ± 0.000007
Mean	126 ± 4	118 ± 6	119 ± 4	114 ± 4	18 ± 3	20 ± 3	0.0802 ± 0.0021	0.0814 ± 0.0017	0.0903 ± 0.0051	0.0913 ± 0.0015				
Mixed meal feeding														
120	140 ± 8	137 ± 7	138 ± 8	131 ± 9	68 ± 13	65 ± 11	0.0797 ± 0.0013	0.0794 ± 0.0011	0.0863 ± 0.0056	0.0894 ± 0.0038	-	-	-	-
180	138 ± 8	139 ± 9	139 ± 8	134 ± 8	72 ± 14	67 ± 11	0.0790 ± 0.0011	0.0802 ± 0.0027	0.0870 ± 0.0069	0.0895 ± 0.0039	-	-	-	-
190	137 ± 8	141 ± 11	139 ± 9	128 ± 9	-	-	0.0790 ± 0.0013	0.0798 ± 0.0011	0.0873 ± 0.0061	0.0890 ± 0.0042	-	-	-	-
200	135 ± 7	142 ± 10	139 ± 9	133 ± 8	-	-	0.0789 ± 0.0014	0.0786 ± 0.0011	0.0863 ± 0.0056	0.0881 ± 0.0042	-	-	-	-
210	138 ± 7	142 ± 11	140 ± 9	132 ± 6	79 ± 17	71 ± 12	0.0778 ± 0.0012	0.0786 ± 0.0011	0.0849 ± 0.0058	0.0863 ± 0.0045	0.0314 ± 0.0015	0.0339 ± 0.0026	0.001578 ± 0.000006	0.001629 ± 0.000013
Mean	138 ± 5	140 ± 6	139 ± 6	132 ± 6	73 ± 10	67 ± 8	0.0790 ± 0.0012	0.0795 ± 0.0011	0.0864 ± 0.0056	0.0885 ± 0.0031				

Diet + Aerobic (N = 11)

Time (min)	Concentration								Enrichment (TTR)					
	Leucine (μ M)		Glucose (mg/dL)		Insulin (μ M/mL)		Plasma α -KIC		Plasma Leucine		Muscle-Free Leucine		Muscle Leucine	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Basal state														
0	128 ± 3	115 ± 5	119 ± 5	109 ± 3	26 ± 5	10 ± 2	-	-	-	-	-	-	-	-
30	-	-	-	-	-	-	0.0733 ± 0.0035	0.0739 ± 0.0035	0.0804 ± 0.0046	0.0812 ± 0.0030	-	-	-	-
40	-	-	-	-	-	-	0.0723 ± 0.0037	0.0730 ± 0.0032	0.0824 ± 0.0044	0.0829 ± 0.0041	-	-	-	-
50	-	-	-	-	-	-	0.0710 ± 0.0038	0.0725 ± 0.0038	0.0800 ± 0.0043	0.0816 ± 0.0038	-	-	-	-
60	129 ± 3	118 ± 4	116 ± 3	109 ± 8	28 ± 6	11 ± 2	0.0710 ± 0.0033	0.0716 ± 0.0036	0.0790 ± 0.0046	0.0818 ± 0.0028	0.0310 ± 0.0022	0.0305 ± 0.0023	0.001518 ± 0.000034	0.001570 ± 0.00021
Mean			118 ± 4	109 ± 4	27 ± 2	11 ± 3*	0.0719 ± 0.0104	0.0728 ± 0.0017	0.0805 ± 0.0041	0.0819 ± 0.0031				

Mixed meal feeding														
120	148 ± 4	144 ± 5	141 ± 5	133 ± 3	60 ± 10	32 ± 8	0.0708 ± 0.0028	0.0704 ± 0.0032	0.0781 ± 0.0071	0.0804 ± 0.0039	-	-		
180	135 ± 7	133 ± 6	141 ± 4	133 ± 8	79 ± 14	34 ± 8	0.0709 ± 0.0029	0.0707 ± 0.0042	0.0783 ± 0.0044	0.0792 ± 0.0042	-	-		
190	136 ± 5	136 ± 8	147 ± 9	136 ± 8	-	-	0.0718 ± 0.0027	0.0708 ± 0.0035	0.0796 ± 0.0040	0.0787 ± 0.0040	-	-		
200	140 ± 6	136 ± 7	143 ± 8	133 ± 8	-	-	0.0710 ± 0.0033	0.0702 ± 0.0036	0.0793 ± 0.0036	0.0794 ± 0.0035	-	-		
210	142 ± 6	139 ± 7	143 ± 8	125 ± 7	77 ± 12	39 ± 9	0.0721 ± 0.0027	0.0701 ± 0.0036	0.0805 ± 0.0036	0.0808 ± 0.0034	0.0319 ± 0.0021	0.0303 ± 0.0026	0.001590 ± 0.000034	0.001656 ± 0.00023
Mean			143 ± 5	132 ± 5	71 ± 9	35 ± 5*	0.0711 ± 0.0020	0.0710 ± 0.0033	0.0790 ± 0.0037	0.0797 ± 0.0035				

Diet + Resistance (N = 12)

Time (min)	Concentration						Enrichment (TTR)							
	Leucine (μM)		Glucose (mg/dL)		Insulin (μM/mL)		Plasma α-KIC		Plasma Leucine		Muscle-Free Leucine			
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After		
Basal state														
0	123 ± 7	119 ± 4	108 ± 4	105 ± 5	17 ± 3	11 ± 2	-	-	-	-	-	-		
30	-	-	-	-	-	-	0.0767 ± 0.0048	0.0731 ± 0.0043	0.0828 ± 0.0074	0.0792 ± 0.0065	-	-		
40	-	-	-	-	-	-	0.0734 ± 0.0044	0.0708 ± 0.0032	0.0811 ± 0.0059	0.0797 ± 0.0057	-	-		
50	-	-	-	-	-	-	0.0723 ± 0.0044	0.0739 ± 0.0053	0.0814 ± 0.0056	0.0788 ± 0.0048	-	-		
60	127 ± 6	125 ± 7	113 ± 4	110 ± 9	18 ± 3	11 ± 2	0.0699 ± 0.0047	0.0713 ± 0.0036	0.0808 ± 0.0057	0.0805 ± 0.0058	0.0316 ± 0.0022	0.0308 ± 0.0079	0.001522 ± 0.000038	0.001597 ± 0.00025
Mean			111 ± 3	107 ± 4	18 ± 2	11 ± 1*	0.0730 ± 0.0021	0.0723 ± 0.0036	0.0815 ± 0.0060	0.0796 ± 0.0054				
Mixed meal feeding														
120	155 ± 5	148 ± 8	133 ± 8	141 ± 5	68 ± 11	46 ± 12	0.0717 ± 0.0047	0.0725 ± 0.0028	0.0811 ± 0.0043	0.0807 ± 0.0041	-	-		
180	145 ± 7	143 ± 8	139 ± 7	137 ± 6	90 ± 14	55 ± 9	0.0724 ± 0.0052	0.0731 ± 0.0033	0.0800 ± 0.0052	0.0808 ± 0.0043	-	-		
190	149 ± 7	136 ± 6	141 ± 7	141 ± 5	-	-	0.0699 ± 0.0047	0.0728 ± 0.0036	0.0806 ± 0.0044	0.0815 ± 0.0045	-	-		
200	142 ± 7	136 ± 2	139 ± 8	135 ± 5	-	-	0.0685 ± 0.0043	0.0728 ± 0.0041	0.0788 ± 0.0036	0.0799 ± 0.00411	-	-		
210	141 ± 7	138 ± 4	136 ± 6	136 ± 5	83 ± 14	51 ± 9	0.0689 ± 0.0039	0.0732 ± 0.0036	0.0808 ± 0.0037	0.0801 ± 0.0042	0.0331 ± 0.0077	0.0311 ± 0.0018	0.001594 ± 0.000036	0.001720 ± 0.000022
Mean			137 ± 5	138 ± 4	80 ± 9	50 ± 7*	0.0708 ± 0.0041	0.0731 ± 0.0033	0.0808 ± 0.0035	0.0806 ± 0.0017				

Diet + Combined (N = 12)

Time (min)	Concentration								Enrichment (TTR)							
	Leucine (μ M)		Glucose (mg/dL)		Insulin (μ M/mL)		Plasma α -KIC		Plasma Leucine		Plasma Leucine		Muscle Leucine			
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Basal state																
0	120 \pm 4	114 \pm 7	110 \pm 6	100 \pm 6	23 \pm 3	14 \pm 2	-	-	-	-	-	-	-	-	-	-
30	-	-	-	-	-	-	0.0781 \pm 0.0045	0.0784 \pm 0.0040	0.0856 \pm 0.0038	0.0866 \pm 0.0049	-	-	-	-	-	-
40	-	-	-	-	-	-	0.0778 \pm 0.0042	0.0768 \pm 0.0032	0.0859 \pm 0.0047	0.0860 \pm 0.0054	-	-	-	-	-	-
50	-	-	-	-	-	-	0.0762 \pm 0.0045	0.0764 \pm 0.0035	0.0869 \pm 0.0047	0.0865 \pm 0.0061	-	-	-	-	-	-
60	124 \pm 4	117 \pm 5	106 \pm 6	106 \pm 4	22 \pm 3	20 \pm 6	0.0755 \pm 0.0045	0.0760 \pm 0.0037	0.0858 \pm 0.0045	0.0879 \pm 0.0039	0.0329 \pm 0.0028	0.0306 \pm 0.0020	0.001468 \pm 0.000018	0.001602 \pm 0.000020	-	-
Mean			108 \pm 5	103 \pm 4	22 \pm 2	17 \pm 3*	0.0769 \pm 0.0021	0.0769 \pm 0.0017	0.0861 \pm 0.0042	0.0868 \pm 0.0049						
Mixed meal feeding																
120	138 \pm 2	137 \pm 3	132 \pm 10	139 \pm 6	78 \pm 17	50 \pm 9	0.0782 \pm 0.0050	0.0747 \pm 0.0036	0.0846 \pm 0.0072	0.0851 \pm 0.0028	-	-	-	-	-	-
180	142 \pm 5	138 \pm 5	135 \pm 7	137 \pm 6	94 \pm 17	46 \pm 7	0.0764 \pm 0.0044	0.0751 \pm 0.0033	0.0851 \pm 0.0048	0.0857 \pm 0.0031	-	-	-	-	-	-
190	137 \pm 5	136 \pm 2	133 \pm 7	131 \pm 7	-	-	0.0772 \pm 0.0042	0.0745 \pm 0.0031	0.0850 \pm 0.0043	0.0861 \pm 0.0030	-	-	-	-	-	-
200	137 \pm 4	136 \pm 3	130 \pm 6	134 \pm 5	-	-	0.0759 \pm 0.0043	0.0772 \pm 0.0044	0.0864 \pm 0.0049	0.0859 \pm 0.0030	-	-	-	-	-	-
210	141 \pm 5	138 \pm 2	127 \pm 6	131 \pm 9	94 \pm 14	47 \pm 7	0.0764 \pm 0.0039	0.0761 \pm 0.0046	0.0862 \pm 0.0055	0.0854 \pm 0.0031	0.0339 \pm 0.0021	0.0337 \pm 0.0017	0.001546 \pm 0.000023	0.001709 \pm 0.000027	-	-
Mean			132 \pm 5	134 \pm 5	89 \pm 11	47 \pm 5*	0.0765 \pm 0.0042	0.0755 \pm 0.0035	0.0854 \pm 0.0047	0.0856 \pm 0.0027						

Values are mean \pm SEM.

* P value <0.05 for comparison with basal state

Table S2. Glucose and insulin response to mixed meal feeding during stable isotope Infusion before and after 6 months of diet-induced weight loss plus different types of exercise interventions in obese older adults. See also Figure 2.

	Control (n = 12)	Aerobic (n = 11)	Resistance (n = 12)	Combined (n =12)
Glucose area under the curve, mg/dl per 2 h				
Baseline	27061 ± 1251	27513 ± 752	26332 ± 1082	25557 ± 1406
Final	27108 ± 1369	26943 ± 950	26365 ± 781	25760 ± 809
Change	47 ± 296	-570 ± 509	64 ± 1120	203 ± 968
Insulin area under the curve, µIU/ml per 2h				
Baseline	10156 ± 1628	10606 ± 1576	11015 ± 1618	12324 ± 2061
Final	9699 ± 1634	5039 ± 999	6945 ± 1254	7362 ± 1083
Change	-457 ± 585	-5567 ± 1962*	-4070 ± 1546*	-4962 ± 1706*
Insulin sensitivity index				
Baseline	5.6 ± 1.9	5.8 ± 0.6	5.2 ± 0.9	5.9 ± 0.8
Final	6.1 ± 1.6	3.0 ± 0.4	2.8 ± 0.4	3.3 ± 0.5
Change	0.4 ± 0.7	-2.8 ± 0.6*	-2.4 ± 0.9*	-2.6 ± 0.6*

Values are mean ± SEM

* P value <0.05 for comparison with Control group

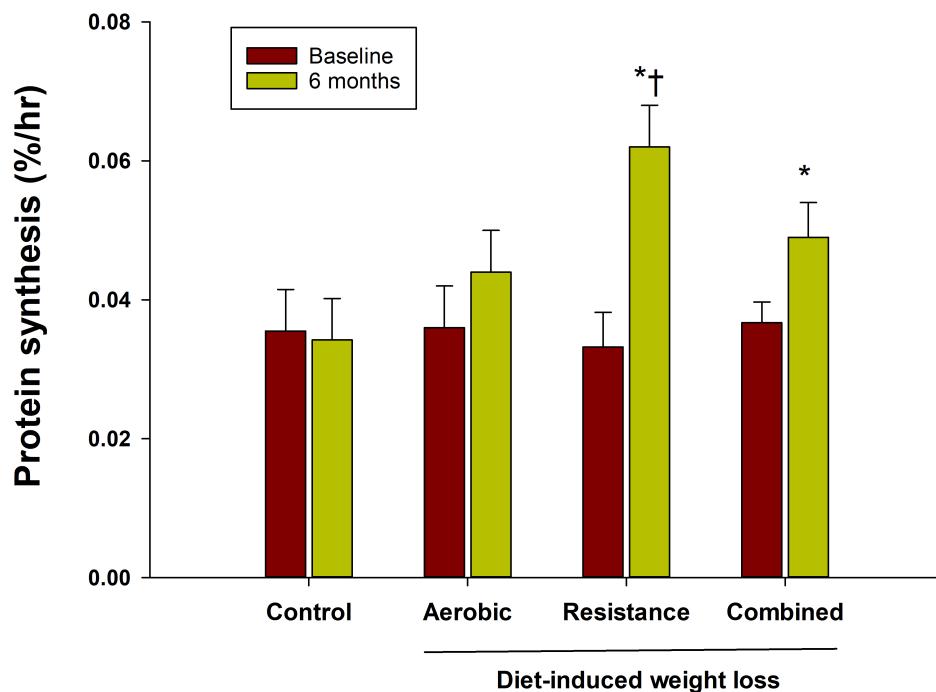


Figure S1.

Muscle protein synthesis rate during mixed meal feeding before and after 6 months of interventions. Muscle protein synthesis rate was calculated using integrated value for plasma leucine isotopic enrichment during the entire period between meals as precursor pool for protein synthesis. Between-group differences in changes in rates of muscle protein synthesis: * p<0.05 for comparison with Control group, † p<0.05 for comparison with Aerobic group. I bars indicate standard errors. n = 11-12/group. See also Figure 2.

Table S4. Tricarboxylic acid metabolites before and after 6 months of diet-induced weight loss plus different types of exercise interventions in obese older adults. See also Figure 3.

Metabolite	Control (n = 8)	Aerobic (n = 8)	Resistance (n = 8)	Combined (n = 8)
Pyruvate				
Baseline	0.0019 ± 0.0003	0.0020 ± 0.0004	0.0018 ± 0.0002	0.0014 ± 0.0003
Final	0.0018 ± 0.0002	0.0016 ± 0.0002	0.0016 ± 0.0002	0.0011 ± 0.0002
Change	-0.0002 ± 0.0001	0.0016 ± 0.0002	-0.0002 ± 0.0003	-0.0003 ± 0.0003
Lactate				
Baseline	3.4863 ± 0.5901	3.8408 ± 0.7584	4.6301 ± 0.8883	4.9854 ± 0.7782
Final	4.364 ± 0.4190	3.9858 ± 0.6988	3.8136 ± 0.9150	5.1623 ± 0.8766
Change	0.8601 ± 0.7057	0.1451 ± 0.5796	-0.8165 ± 1.1543	0.1769 ± 1.2150
Citrate/Isocitrate				
Baseline	0.9774 ± 0.1423	1.1012 ± 0.1932	0.5877 ± 0.0834	0.5689 ± 0.0810
Final	0.8038 ± 0.0819	0.7050 ± 0.0954	0.7649 ± 0.0684	0.5475 ± 0.0918
Change	-0.1736 ± 0.1577	-0.3962 ± 0.1921	0.1771 ± 0.1083	-0.0214 ± 0.0868
Cis-aconitate				
Baseline	0.2538 ± 0.0297	0.2259 ± 0.0310	0.2496 ± 0.0397	0.3220 ± 0.0336
Final	0.3318 ± 0.0175	0.2521 ± 0.0334	0.2190 ± 0.0342	0.3254 ± 0.0422
Change	0.0780 ± 0.1577	0.0263 ± 0.0199	-0.0305 ± 0.0459	0.0034 ± 0.0574
Ketoglutarate				
Baseline	0.2562 ± 0.0398	0.3023 ± 0.0147	0.2789 ± 0.0270	0.2703 ± 0.0340
Final	0.3062 ± 0.0171	0.2679 ± 0.0263	0.2661 ± 0.0237	0.2034 ± 0.0226
Change	0.0500 ± 0.0256	-0.0344 ± 0.0237	-0.0128 ± 0.0330	-0.0669 ± 0.0267
Glutamic acid				
Baseline	6.7105 ± 0.8286	6.2490 ± 0.6186	5.0144 ± 0.4787	5.2189 ± 0.5183
Final	5.6743 ± 0.5344	5.7410 ± 0.4949	5.0914 ± 0.9073	4.5217 ± 0.6199
Change	-1.0361 ± 0.4163	-0.5080 ± 0.6988	0.0770 ± 0.8386	-0.6971 ± 0.5711
Glutamine				
Baseline	5.5805 ± 0.4556	5.4243 ± 0.3228	5.2850 ± 0.4671	5.3451 ± 0.4588
Final	5.8570 ± 0.3451	5.4306 ± 0.4753	5.0997 ± 0.3532	4.7259 ± 0.5672
Change	0.2764 ± 0.2453	0.0062 ± 0.5850	-0.1852 ± 0.5640	-0.6192 ± 0.6223
Succinate				
Baseline	0.1491 ± 0.0365	0.1075 ± 0.0212	0.1086 ± 0.0185	0.1136 ± 0.0151
Final	0.1567 ± 0.0376	0.2369 ± 0.0447	0.1317 ± 0.0236	0.1344 ± 0.0238
Change	0.0076 ± 0.0413	0.1294 ± 0.0473*	0.0231 ± 0.0224	0.0209 ± 0.0212
Fumarate				
Baseline	0.0447 ± 0.0053	0.0496 ± 0.0045	0.0423 ± 0.0042	0.0389 ± 0.0029
Final	0.0529 ± 0.0080	0.0523 ± 0.0085	0.0391 ± 0.0052	0.0391 ± 0.0052
Change	0.0082 ± 0.0071	0.0027 ± 0.0108	-0.0033 ± 0.0026	-0.0020 ± 0.0036
Malate				
Baseline	3.9422 ± 0.6582	4.2176 ± 0.4383	4.1166 ± 0.5077	4.8132 ± 0.6125
Final	5.2032 ± 0.8750	4.2479 ± 0.7105	4.4931 ± 1.0237	4.2448 ± 0.6258
Change	1.2610 ± 0.7227	0.0304 ± 0.7857	0.3764 ± 0.9376	-0.5684 ± 0.7199

Oxaloacetate				
Baseline	0.0034 ± 0.0009	0.0037 ± 0.0006	0.0032 ± 0.0002	0.0029 ± 0.0002
Final	0.0032 ± 0.0003	0.0033 ± 0.0006	0.0029 ± 0.0003	0.0030 ± 0.0003
Change	-0.0002 ± 0.0007	-0.0004 ± 0.0007	-0.0003 ± 0.0003	0.0000 ± 0.0004

Values are normalized intensity mean ± SE.

* P value <0.05 for the comparison with the Control group

